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| (54) Title: CALCAREOUS MATERIAL (57) Abstract Calcareous materials which are very purified residues of corallinaceae particularly Lithothamnium corallioides have unusual therapeutic properties including treatment of conditions created by failure of immune regulation for example rheumatoid or osteo arthritis, osteoporosis and other conditions involving pH control. A method for purification is provided. Also provided are compositions of said residues together with fatty acids, glycerides, polyglycols and emulsifiers. Particularly advantageous are compositions of the residues and medium chain triglycerides. | | |

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CALCAREOUS MATERIAL

This invention relates to calcareous materials from natural organic sources and particularly compositions comprising residues of corallinaceae for example Lithothamnium corallioides for use in the therapeutic treatment of humans or animals. The invention also relates to the use of said materials in foodstuffs and processing of foodstuffs.

10

Corallinaceae, for example Lithothamnium corallioides, are known seaweeds which are very abundant in certain cold and temperate seas. Once harvested the crude residual product consists primarily of mineral substances, particularly calcium carbonate and magnesium carbonate. The largest component is calcium carbonate, often about 34% by weight. This product is sometimes identified as Maërl though the term Maërl encompasses residues of coralline algae of various members of the order corallinales (Class Rhodophyceae) including members of corallinaceae for example members of the species Lithothamnium corallioides, Phymatolithon calcareum and Lithothamnium glaciale.

Crude corallinaceae (Lithothamnium corallioides) residues have been commercially available for use in the prevention of acidosis in intensively fed cows. In French patent FP2 201 040 there is disclosed the use of Maërl which appears to be in the crude form for animal feeds. Such products as have been available until the present time have tended to be relatively impure products frequently from contaminated sources. Usually they contain significant amounts of siliceous materials derived from the original product as dredged and other non-corallinaceae residues for example ground shells of sea-creatures.

35

The Institute of Oceanography in Paris produced a report on corallinaceae particularly Lithothamnium in 1989

describing the residual crude product (Maërl) and describing its use in treatment of soil and for animal feed as a dietary supplement and for treatment of water.

- 5 The subject invention provides further medical uses for compositions comprising residue of corallinaceae (Maërl) in highly purified form.

10 Corallinaceae particularly Lithothamnium corallioides are coralline algae. There are a number of sub-species of corallinaceae particularly Lithothamnium differentiated by morphological data but these data can vary depending on local sea bed and weather conditions. Other known "relatives" include Phymatolithon calcareum and in more
15 northerly regions Lithothamnium glaciale. These plants lay down calcium carbonate in their cell walls which gives them a hard stony texture. The living corallinaceae for example Lithothamnium corallioides generally show a red colour due to the presence of a pigment phycoerythrin in
20 their structure. When dead the colour is white or yellowish. Corallinaceae for example Lithothamnium corallioides occurs naturally in cold and temperate seas and has been reported in Norway, Canada, Scotland, Ireland and France.

25

 Since compositions of the subject invention are to be used therapeutically it is of course important that the corallinaceae which is to be exploited in the invention is derived from a part of the world which does not suffer from
30 heavy pollution. For this purpose corallinaceae particularly Lithothamnium corallioides harvested from stocks north of Lonehort Point, Castletownbere, County Cork in the Republic of Ireland have proved very satisfactory but there are also deposits off the West Coast of Galway.

35

 In the concentrated and purified form of the invention the residue of corallinaceae has proved particularly

effective for use in a composition for the manufacture of medicament for the treatment of disorders arising from immunoregulation problems. These problems are, for example, rheumatoid arthritis, osteo arthritis, gout, 5 raised cholesterol levels, period pains, reduced body fluid pH levels, osteoporosis, incipient ulcerative conditions, and certain conditions sometimes described as "low energy" or chronic fatigue problems. Also the product is applicable to reduced calcium level problems and raised pH 10 levels in the colon and certain indigestion problems.

Naturally occurring residues of Lithothamnium corallioides were harvested at the above site at Lonehort Point, purified, concentrated and formed into capsules 15 containing 0.5 grammes of concentrate.

The raw material can be purified by initial extensive washing with sea and fresh water together with removal of extraneous sand, shells, and other debris particularly 20 siliceous debris such as stones. This step usually reduces the material obtained by dredging from the sea bed to about 20% by weight.

The cleaned and separated product is then subjected to 25 intensive cleaning by for example, bleaching and sterilising in hydrogen peroxide for from 8 to 24 hours, further washing in water, drying in a sterile fluid bed and final milling under bacterial controlled conditions.

30 The stringent washing conditions reduce sodium content of the raw product from amounts in the order of well in excess of 1,000 ppm for example amounts up to 5,200 ppm to sodium contents in the low hundreds, for example 300 ppm. Thus there is a reduction of about 10 fold in the sodium 35 content as compared to raw material.

The silica content of this final material is normally

not more than 0.5% by weight as compared to a silica content in previously available Maërl from a commercial source, of about 5% by weight.

- 5 The product is packaged by aseptic formation into capsules, tablets or emulsions.

A representative sample of this purified, concentrate contained the following elements in the following amounts

10

| | | |
|----|-------------|----------|
| | Calcium | 34% |
| | Magnesium | 2.4% |
| | Phosphorous | 0.08% |
| | Potassium | 0.10% |
| 15 | Sulphur | 0.45% |
| | Iron | 20 ppm |
| | Boron | 16.5 ppm |
| | Sodium | 300 ppm |
| | Manganese | 125 ppm |
| 20 | Cobalt | 6 ppm |
| | Copper | 10 ppm |
| | Zinc | 37 ppm |
| | Selenium | 1 ppm |
| | Molybdenum | <3 ppm |
| 25 | Iodine | 160 ppm |
| | Arsenic | <1 ppm |
| | Lead | <1 ppm |
| | Chromium | 13 ppm |
| | Cadmium | 0.2 ppm |
| 30 | Mercury | <50 ppb |
| | Aluminium | <1 ppm |

One possible reason for the activity of this material is the availability of mineral elements. These serve the
35 physiology of the body in various ways for example;

- (a) constituents of skeletal structure;
- (b) regulation of physical properties of colloidal systems
40 (viscosity, diffusion, osmotic pressure);
- (c) acid-base regulators; and
- (d) components and activators of enzymes and other active

biological systems.

Thus the calcium from the product of the invention may assist in:

5

(i) blood coagulation;

(ii) muscle irritability;

10

(iii) myocordial function;

(iv) control of acetylcholine (neuromuscular irritability); and

15

(v) enzyme activation

The magnesium content may be of benefit in relation to over 300 enzymatic reactions including carbohydrate utilisation, ATP metabolism, muscle contraction, nerve impulse conduction, transmembrane ion transport, enzyme activation particularly in relation to utilisation of vitamins B1, B2, B6, C and E, and synthesis of fat, protein and nucleic acids. The composition may assist in providing an Na/calcium balance and also may affect the potassium balance. In addition the content and availability of metals such as copper, iron, cobalt, zinc and other components in the product may have effects on physiological and biochemical systems in the body which would not have been anticipated from the mere analysis of the raw material. For example, the copper content may assist with connective tissue dysfunctions, bone fragility, cardiovascular disorders and defects in the lysyl oxidase function. The zinc content may assist with defects in the over 70 enzymatic systems in which zinc is a cofactor.

35

Rat feeding trials have been conducted with the concentrate to assess the safety of the product in humans.

These trials were completely satisfactory.

Pharmaceutically effective amount of the corallinaceae residues can be used in the methods of the invention.

5

For example patients being treated with the concentrate can be dosed with from 0.5 grammes to 3 grammes of concentrate per day.

10 Compositions comprising effective amounts of the purified concentrate are useful inter alia for the treatment of conditions involving failure of immuno regulations and include rheumatoid and osteo arthritis, gout, high cholesterol, period pains, low body fluid pH,
15 osteoporosis, and incipient ulcerative conditions of the type which have been successfully treated with antiulcer drugs (such as Tagamet, Zantex, Losec (all are Registered Trade Marks)). An important aspect is treatment of chronic fatigue problems and the achieving of a feel good factor.

20

Such compositions can also be used for the treatment of indigestion. Furthermore such compositions can be used to treat low calcium levels. A dosage of three 0.5 gramme capsules per day supplies 480 milli-grammes a day of
25 calcium to the patient.

Furthermore such compositions can be used to treat ulcerative conditions of the colon. It is theorised that such treatments result in elevation of colon pH and
30 subsequent suppression of Helicobacter pylori.

Such compositions have also been effective in treating hangovers.

35 Another aspect of the invention is the combination of the purified residues of corallinaceae with fatty acids or polyols. The unusually porous structure of the

Corallinaceae product which will hereinafter for convenience be referred to as the Calcium Product is advantageous over other natural calcium sources in allowing the absorption of fatty acids and glycerides as well as polyols to allow a product which is still flowable.

In particular the calcium product is advantageous when combined with functional polyunsaturated fatty acids (PUFAs) also known as omega-long-chain-fatty acids (LCFAs). These fatty acids are of growing interest in the fortification of food formulae particularly those for children.

According to the invention there is provided a composition comprising the combination of a residue in very pure form of a corallinaceae (Maërl) and a fatty acid, a glyceride or a polyglycol.

There is also provided a composition comprising the combination of a residue in very pure form of corallinaceae (Maërl) and an emulsifier.

There is further provided a method of forming emulsions in the manufacture of foods wherein an emulsifier is combined with a residue in very pure form of corallinaceae (Maërl) and simultaneously or subsequently with an oil phase of a food stuff and thereafter an emulsion is formed with an aqueous phase.

Omega-LCFAs are divided into two families:

Omega-6: ARA (arachidonic acid) from plant and animal fats.

Omega-3: EPA (Eicosapentaenoic acid) and DHA (docosahexaenoic acid) from fish oils and algae.

ETA (Eicosatetraenoic acids) extracted from the New Zealand Green-Lipped Mussels (*Perna Canalicus*).

5 The omega-3 family has been shown to be essential for normal biological functions. EPA plays an important role in the regulation of inflammatory immune reactions and blood pressure: it is a precursor of prostaglandin E3 that inhibits blood clots.

10

DHA is required for the optimal development of the nervous system and maturation of visual acuity in preterm and full term infants. DHA is the most highly unsaturated fatty acid found in nature and the predominant structural
15 fatty acid in the brain (40%) and retina (60%). It was also shown to have significant effects at the auto-immune system.

ETA are a unique family involved in joint inflammation
20 prevention and treatment. They act as potent nutritional inhibitors of the lipxygenase pathway, which are responsible for leukotrienes production.

Other products comprise MCT (Medium chain
25 triglycerides: C6, C8 and C10) that are involved in the reduction of mortality of premature new born infants weighing <1.5 Kg or piglets during the weaning age.

Omega-3 fatty acids and MCT have in common the fact
30 they are all in oil form. It has been proposed to stabilise these lipids so as to produce and protect marine oils for food fortification use (bakery products, milk powder). There has been suggestion of incorporating into soft gel capsules for the health products market.

35

The Calcium Product of the invention offers an unusually effective alternative to the above techniques of

presentation because of its highly porous structure. This highly porous structure provides a high specific structure on the same particle size of 9m^2 as against 1.7m^2 for calcium carbonate in more conventional forms. This porous structure can be demonstrated using a scanning electron microscopic technique. The Calcium Product of the invention allows the possibility of combining with the above lipid products without affecting the particle size or the flowability of the final product. The precise relationship will depend on the nature of the lipid compound and the molecular weight which bears upon the relationship to the pore size of the Calcium Product.

The products have a neutral taste (probably because of the absorption into the pores of the Calcium Product. Absorption of 5 to 15% by weight gives a very useful product.

Thus the product of the invention provides the possibility of a combination of MCT and a calcium product as a calcium source for baby food. Also there is provided the possibility of a combination of omega-3 LCFA's (EPA, DHA and DTA) as a calcium source for food fortification intended for children and adults.

Combinations of the invention comprising the Lithothamnium corallioides residues (the Calcium Product) and MCT's are particularly of interest.

Generally fats, or lipids, perform a variety of functions including energy storage, membrane structure and incorporation in vitamins, hormones and prostaglandins. Triglycerides are the most common form of fat. Triglycerides comprise three fatty acids esterified to a glycerol backbone. Most naturally occurring triglycerides contain fatty acids 16-20 carbon atoms in length. Such fatty acids are called "long chain fatty acids" (LCFAs),

and their corresponding triglycerides are called "long chain triglycerides" (LCTs). Medium chain triglycerides (MCTs) comprise medium chain fatty acids (MCFAs), which are 6-12 carbons in length. Although the carboxylic acid part of fatty acids is soluble in water, the hydrocarbon chain is not. Thus, LCFAs are not water soluble. Since the hydrocarbon chains of MCFAs are shorter, MCFAs are more water soluble than LCFAs. Likewise, MCTs are also relatively soluble in water, due to ionization of the carboxylic acid groups and the small size of the hydrocarbon chains. Their small molecular size and greater water solubility cause MCTs to undergo a different metabolic path than that experienced by LCTs.

Medium chain triglycerides occur naturally in small quantities in a variety of foods, including human milk. In cow's milk, C6-C14 fatty acids together account for 20% of the total fatty acid composition. Commercially medium chain fatty acids are prepared by the hydrolysis of coconut oil and fractionate up by steam distillation. The MCFAs so obtained consist of predominantly C8 with lesser amounts of C10 and minute amounts of C6 and C12. The fractionated MCFAs can be re-esterified with glycerol to generate MCTs.

MCTs have been used for fat malabsorption problems and have been widely used in enteral and parenteral nutrition. Use of the MCT's permits provision of calories in a more readily oxidisable form and less interference with the RES component of the immune system. Recently athletes have begun to use MCT's to provide energy and facilitate weight gain.

In metabolism the solubility of the MCFA's avoids a complicated digestive process found with LCT's. The MCT's are readily degraded within the intestine into free MCFA's and glycerol. Therefore as compared to conventional fats MCT's are transported directly to the liver and used for

energy rather than being stored in cells. This indicates the desirability of MCT's as components of foodstuffs to avoid deposition of fats. MCT's therefore have been incorporated into diets particularly for sports persons.

5 An example is the interest in goats milk which contains higher content of MCT's as compared to cow milk.

Thus capric, caprylic and other MCT's have been used for the treatment of malabsorption syndrome, intestinal

10 disorders, coronary diseases, premature infant nutrition, cystic fibrosis and gallstone problems because of the capacity to provide energy and possibly dissolve cholesterol deposits. Similarly coconut products, particularly coconut oil which is an excellent source of

15 medium-chain triglycerides has received much attention.

Methods of incorporating MCT's more effectively into the diet by combination with absorbants are therefore of considerable interest and the discovery that the Calcium

20 Product of the invention affords a excellent means of absorbing MCT's is of great significance.

Another aspect of the invention is the combination of the Calcium Product with polyols such as glycerol,

25 monopropylene glycol and viscous polyols alone or with other functional products. Such products comprising a combination of a monoglyceride and the Calcium Product of the invention could be a calcium source for bakery products, bread, toppings, margarine and spreads,

30 chocolates and all calcium fortification products employing monoglycerides as emulsifiers. Combining Calcium Product with emulsifiers, particularly glycerides, would provide a new range of products for calcium fortification and emulsification. The emulsifiers are preferably those

35 having properties analogous to glycerides but the invention applies to emulsifiers used in the food industry particularly to stabilise oil/water emulsions.

The combination of the Calcium Product and polyols, glycols, mono-or di-glycerides and emulsifiers generally simplifies the introduction of the emulsifier. It has been found that, if the emulsifier is incorporated into the Calcium Product and simultaneously or subsequently with an "oil phase" the formation thereafter of an emulsion with an aqueous phase gives an improved emulsion of greater stability.

The combination of the calcium product and the fatty acid or polyol can be carried out by any of the standard techniques for combining solid carrier and materials such as fatty acids, glycerides and polyols. It is preferred to use one of the following techniques:

Air suspension coating, known also as fluidised bed processing or spray coating. The bed is sprayed with a coating solution. The coating dries on the core powder to form a film of a certain thickness.

Spray chilling and spray cooling; The coating substance can be a derivative of vegetable or other encapsulating materials, i.e. stearine with melting points of 45°C to 122°C as well as mono and diglycerides with melting points of 45°C to 67°C. The coated material is obtained by nebulising the coating substance with heated nozzles into a chamber containing cool air. The reduction of temperature results in solidification of the lipid coat.

Differential Scanning Calorimetry (DSC) can be used to monitor changes in physical or chemical properties of materials as a function of temperature by detecting the heat changes associated with such processes.

The invention is illustrated by the accompanying drawings in which:

Figure 1 is a distribution of particle sizes on the introduction of MCT measured on a "HELOS" (Trade Name) laser particle size determination apparatus (Example 9), i.e. analysis on dry form of coated "Calcium Product" with 0%; 5%; 10%; 12% and 15% MCT.

Figure 2 is a "HELOS" laser particle size analysis on wet form of coated "Calcium Product" with 0%; 5%; 10%; 12% and 15% MCT (Example 9).

Figures 3 and 4 illustrate "HELOS" laser particle size analysis on dry or wet form, respectively, of coated "Calcium Product" with 10% emulsifier (and 5% for sorbitan) (Example 10).

Figures 5 and 6 illustrate "HELOS" laser particle size analysis on dry or wet form, respectively, of coated "Calcium Product" and CaCO_3 with 10% Monoglyceride (MP:35-40°C).

The Calcium Product employed is a commercial product prepared from Lithothamnium corallioides residues as described above and having the analysis set out above.

More than 300 human volunteers were found and dosed three times a day with capsules containing 0.5 grammes of purified concentrate of Lithothamnium corallioides residue from dredging at Lonehort Point.

Some of the results are reported in the following Examples.

Example 1

One group of volunteers suffered from rheumatoid and osteo arthritis.

It was found that depending on age, greatly improved mobility was experienced with the above daily consumption preferably with meals. Younger patients experienced relief within 3 weeks, whereas older patients and particularly those in the 70/80 age bracket took 8/12 weeks to show substantial improvement.

Once achieved, daily consumption was necessary to

ensure maintenance of enhanced mobility.

Example 2

Another group of volunteers suffered from gout. These
5 volunteers were dosed in the same way as above.

It was found that complete elimination of gout
symptoms occurred within a few days of use in 90% of trial
participants.

10

From laboratory results it appears that the uric acid
is maintained in a molecular condition, which precludes
deposition.

15 Example 3

A further group of volunteers were dosed as above.
Cholesterol levels were found to have been reduced with a
drop from for example 6.8/7.5 to 5.2/5.4 being possible in
about 40% of subjects.

20

Example 4

A further group of volunteers were dosed as above. It
was found that period pains could be totally eliminated and
that premenstrual tension could be reduced.

25

Example 5

Patients were dosed as above and it was shown that
body fluid pH (as determined by salivary pH levels) could
be adjusted to and maintained at 6.8-7.0 which is the
30 generally accepted optimum body fluid pH.

Example 6

Patients were dosed as above and it was shown that
indole and sulphite residues were eliminated in the urine.

35

Example 7

Patients were dosed as above and it was shown there

was a lowering of triglyceride levels in the blood.

Example 8

Patients were dosed as above and it was shown there
5 was an increase in urine production i.e. that there was
water diuresis result (dehydration).

Compositions comprising purified residue in Lithothamnium
Corallioides

10

Example 9

Combination with medium chain triglycerides (MCT)

MCT is a low viscous oil, almost colourless from
15 caprylic (C8) and capric (C10) vegetable fatty acids.

A Calcium Product was prepared by purification of
Lithothamnium corallioides harvested at Loenhort Point
described above (Calcium Product).

20

Initial trial work showed that Calcium Product maximum
oil absorption capacity was 64%. At this level the
flowability was lost, the product being in the paste form.
The optimum level of MCT absorption compatible with
25 flowability using an air suspension coating technique was
readily determinable.

Calcium Product was coated with 5%, 10%, 12% and 15%
MCT.

30

Figure 1 shows a regular increase of the particles
size according to the level of MCT, below 90% distribution.
Above 90% there is a derivation due to some aggregates
(analysis of non sieved coated product). This is confirmed
35 by Figure 2 on wet product analysis: the aggregates are
disrupted. Globally, the particles size remain below 3um.

The 5% coating gave 2 density peaks close to those of the control. The coating was not obviously sufficient to agglomerate the finest particles. From 10 to 15% coating there was a unique density peak.

5

Example 10Tests with different emulsifiers

10 A Calcium Product as described above was combined with various emulsifiers as follows:

| | <u>Emulsifier</u> | <u>Melting Point °C</u> | <u>Sample Nos.</u> |
|----|-------------------|-------------------------|--------------------|
| | Sorbitan | 20 | (1) 5% (2) 10% |
| 15 | Monoglyceride 1 | 35-40 | 3 |
| | Fatty Alcohol | 55-58 | 4 |
| | Monoglyceride 2 | 68-70 | 5 |
| | Triglyceride 1 | 52-53 | 6 |
| | Triglyceride 2 | 58 | 7 |
| 20 | | | |

The samples were coated at 10% by weight except for Sorbitan: 5% and 10%.

25 The analysis were done again on the non sieved treated products. The most flowable ones were with the 2 monoglycerides. The laser particles size analysis do not clearly reveal that point (figures 3 & 4) except for Figure 4 on wet form.

30

The DSC analysis results clarify the interaction between the tested emulsifiers and Calcium Product.

35 Calcium Product coated samples were analysed by DSC in the range of temperature 5 to 125°C using a rate of heating of 5°C/min. A first series of data were obtained in these conditions. Results are shown in Table 1.

TABLE 1

| Glass Transition | | Melting | | | | | | Recrystal |
|------------------|-----|------------------------|-----------------------|---------------------|------------------------|-----------------------|---------------------|-----------|
| Tg1 | Tg2 | Melting 1 | | | Melting 2 | | | Tr |
| | | T _m onset 1 | T _m peak 1 | ΔH_f1 (J/g) | T _m onset 2 | T _m peak 2 | ΔH_f2 (J/g) | |

| | | | | | | | | |
|---|--------|--------|--------|-------|---------|--------|-------|---------|
| 1 | 53, 54 | | | | | | | |
| 2 | 26, 77 | 36, 88 | | | | | | |
| 3 | 24, 34 | | 32, 34 | 35, 3 | -2, 494 | | | 20 |
| 4 | 50, 61 | | 61, 06 | 63, 1 | -5, 984 | | | 45 |
| 5 | 39, 78 | | 68, 43 | 71, 4 | -2, 674 | | | 35, 5 |
| 6 | 31, 27 | | 51, 07 | 56, 4 | -4, 494 | | | 26, 7 |
| 7 | | | 50, 57 | 53, 7 | -3, 789 | 58, 47 | 62, 4 | -4, 577 |

Thermograms were interpreted as melts when the endothermal peaks of melting are well defined with an onset
5 and a peak temperature of melting. Glass transitions (T_g) were also derived from the thermograms showing a change in heat flow with a slope of baseline unchanged. Some samples show polymorphism behaviour with 2 melting endotherms. When an endotherm is observed it is assigned to a
10 recrystallisation.

In a second series of analyses all samples were heated rapidly ($10^\circ\text{C}/\text{Min}$) to 120°C , then cooled rapidly to -10°C . DSC analysis was performed on these annealed samples at a
15 rate of $5^\circ\text{C}/\text{min}$. Results are shown in Table 2.

20

25

30

35

TABLE 2

| Glass Transition | | Melting | | | | | | Recrystal |
|------------------|-----|------------------------|-----------------------|-----------|------------------------|-----------------------|------------|-----------|
| | | Melting 1 | | | Melting 2 | | | |
| Tg1 | Tg2 | T _m onset 1 | T _m peak 1 | ΔHf1(J/g) | T _m onset 2 | T _m peak 2 | ΔHf2 (J/g) | |
| | | | | | | | Tr | |

| | | | | | | | | | |
|---|-------|-------|-------|------|--------|-------|----|-------|--|
| 1 | 41,41 | | | | | | | | |
| 2 | 38,88 | | | | | | | | |
| 3 | | | 22,1 | 27,1 | | | | | |
| 4 | 23,52 | 54,68 | 59,78 | 61,8 | -2,698 | | | 19,1 | |
| 5 | | | 67,74 | 70,9 | -5,308 | | | | |
| 6 | | | 49,67 | 56 | -4,264 | | | | |
| 7 | | | 50,22 | 52,9 | -3,245 | 58,51 | 62 | -3,99 | |

It may be observed that erasing the thermal history of samples by annealing eliminates a number of pseudo-thermal events, especially as concerns Tg and recrystallisation. The polymorphism of a product containing triglyceride 2 was confirmed and the melting points of different samples was verified, except for monoglyceride 1 which showed an endotherm at lower temperature (22-27°C) after annealing than before. This indicates a unique interaction between Calcium Product and low melting point monoglyceride.

Monoglycerides gave good thermograms and the coated materials were free flowing, which was not the case with the other products.

Example 11

Comparison between Calcium Product and Calcium Carbonate

A Calcium Carbonate was employed from a normal commercial source.

The Calcium Product of the invention and Calcium Carbonate were coated with 10% monoglyceride-1.

The coating was done with 10% monoglyceride-1. Calcium Product gave a homogeneous product. The taste was neutral and corresponded to that of the original Calcium Product. Calcium carbonate gave a heterogeneous product, non flowable and produced large particles (Figure 5). The taste was chalky and also revealed the typical emulsifier taste. This is an indication of the presence of three populations: Calcium Carbonate (pure and coated) and free emulsifier.

The wet form analysis (Fig. 6) revealed the presence of fine particles below 8µm. These come from the crystallised emulsifier. The distribution curve recovers its initial form from 50%. It shows a complete separation

between the emulsifier and the carrier. The absence of porosity explains the behaviour of calcium carbonate with monoglyceride.

- 5 Calcium Product gave a completely different figure with the curve of the coated material remaining above the control.

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CLAIMS:

1. Use of a composition comprising the residue in very pure form of corallinaceae for the manufacture of a medicament for the treatment of conditions created by a failure of immuno regulation in the body.
2. Use according to claim 1 wherein the corallinaceae residue is the residue of Lithothamnium corallioides.
3. Use according to either of claims 1 or 2 in which the sodium content of the raw material is reduced by at least ten fold in the purification.
4. Use according to claim 3 in which the sodium content is reduced into the low hundreds ppm by weight.
5. Use according to any one of claims 1 to 4 in which the silica content of the residue has reduced to about 0.5% or less by weight.
6. Use according to any one of claims 1 to 5 in which the condition is arthritis particularly rheumatoid or osteo arthritis.
7. Use according to any one of claims 1 to 5 in which the condition is gout.
8. Use according to any one of claims 1 to 5 in which the condition is raised cholesterol levels.
9. Use according to any one of claims 1 to 5 in which the condition is period pains.
10. Use according to any one of claims 1 to 5 in which the condition is osteoporosis.

11. Use according to any one of claims 1 to 5 in which the condition is chronic fatigue.
12. Use of a composition comprising the residue in very
5 pure form of corallinaceae (Maërl) for the manufacture of a medicament for the treatment of conditions created by reduced body fluid pH level.
13. Use of a composition comprising the residue in very
10 pure form of corallinaceae (Maërl) for the manufacture of a medicament for the treatment of incipient ulcerative conditions.
14. Use of a composition comprising the residue in very
15 pure form of corallinaceae (Maërl) for the manufacture of a medicament for the treatment of indigestion.
15. Use of a composition comprising the residue in very
pure form of corallinaceae (Maërl) for the manufacture of
20 a medicament for the treatment of reduced calcium levels.
16. Use of a composition comprising the residue in very
pure form of corallinaceae (Maërl) for the manufacture of
a medicament for raising pH levels in the colon.
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17. Use of a composition comprising the residue in very
pure form of corallinaceae (Maërl) for the manufacture of
a medicament for the treatment of hangovers.
18. Use according to any one of claims 12 to 17 in which
30 the corallinaceae residue is the residue of Lithothamnium corallioides.
19. Use according to any one of claims 12 to 18 in which
35 the sodium content of the raw material is reduced by at least ten fold in the purification.

20. Use according to claim 19 in which the sodium content is reduced into the low hundreds ppm by weight.
21. Use according to any one of claims 12 to 20 in which
5 the pure form of the residue has a silica content of about 0.5% by weight or less.
22. A method of forming a form of corallinaceae for medical treatment of human or animals in which siliceous
10 materials and debris are removed from a dredged product, the product is intensively washed, then the product is bleached, cleansed and sterilised particularly by hydrogen peroxide and dried and packaged under sterile conditions.
- 15 23. A method according to claim 22 in which washing is effected to lower the sodium content by ten fold to a figure in the low hundreds ppm.
24. A composition comprising the combination of a residue
20 in very pure form of a corallinaceae (Maërl) and a fatty acid, a glyceride or a polyglycol.
25. A composition comprising the combination of a residue in very pure form of corallinaceae (Maërl) and an
25 emulsifier.
26. A composition according to either of claims 24 or 25 in which the residue is the residue of Lithothamnium corallioides.
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27. A composition according to either of claims 24 or 26 wherein the fatty acid is a functional polyunsaturated fatty acid.
- 35 28. A composition according to claim 27 wherein the acid is ARA, EPA, DHA or ETA.

29. A composition according to either of claims 24 or 26 in which glyceride is a medium chain triglyceride of 6 to 10 carbon atoms.

5 30. A composition according to either of claims 24 or 26 in which the polyol is glycerol or monopropylene glycol.

31. A method of forming emulsions in the manufacture of foods wherein an emulsifier is combined with a residue in
10 very pure form of corallinaceae (Maërl) and simultaneously or subsequently with an oil phase of a food stuff and thereafter an emulsion is formed with an aqueous phase.

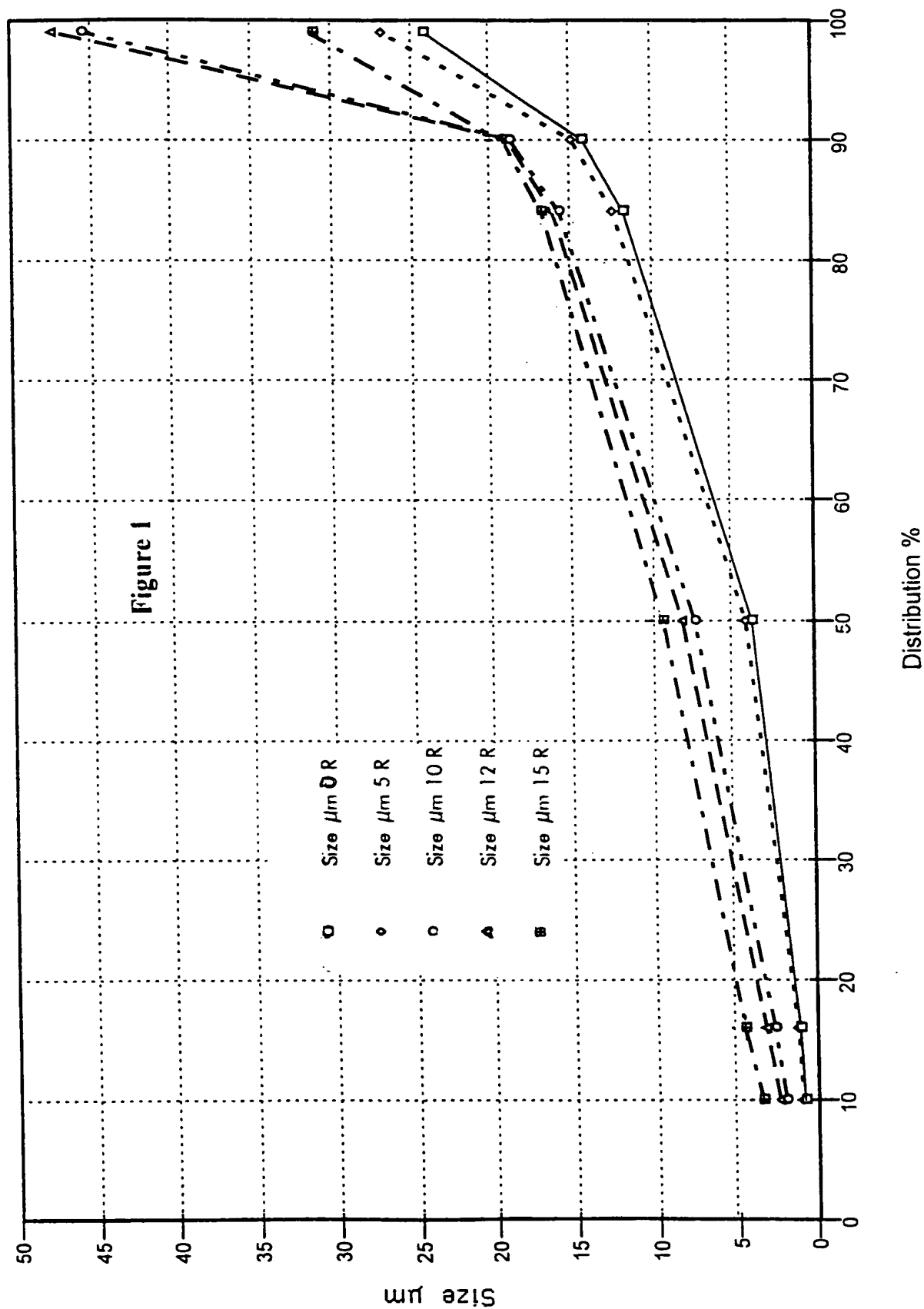
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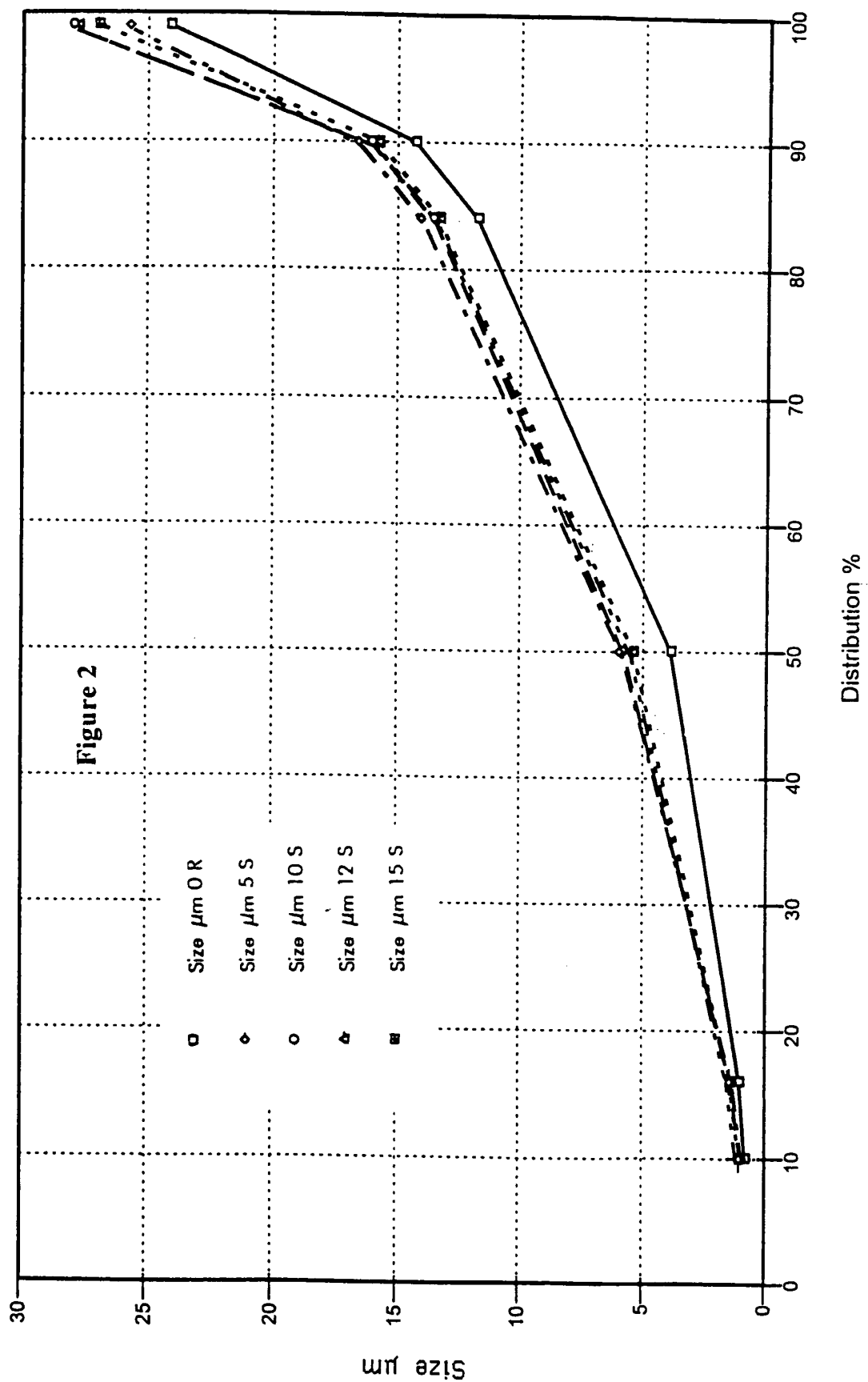
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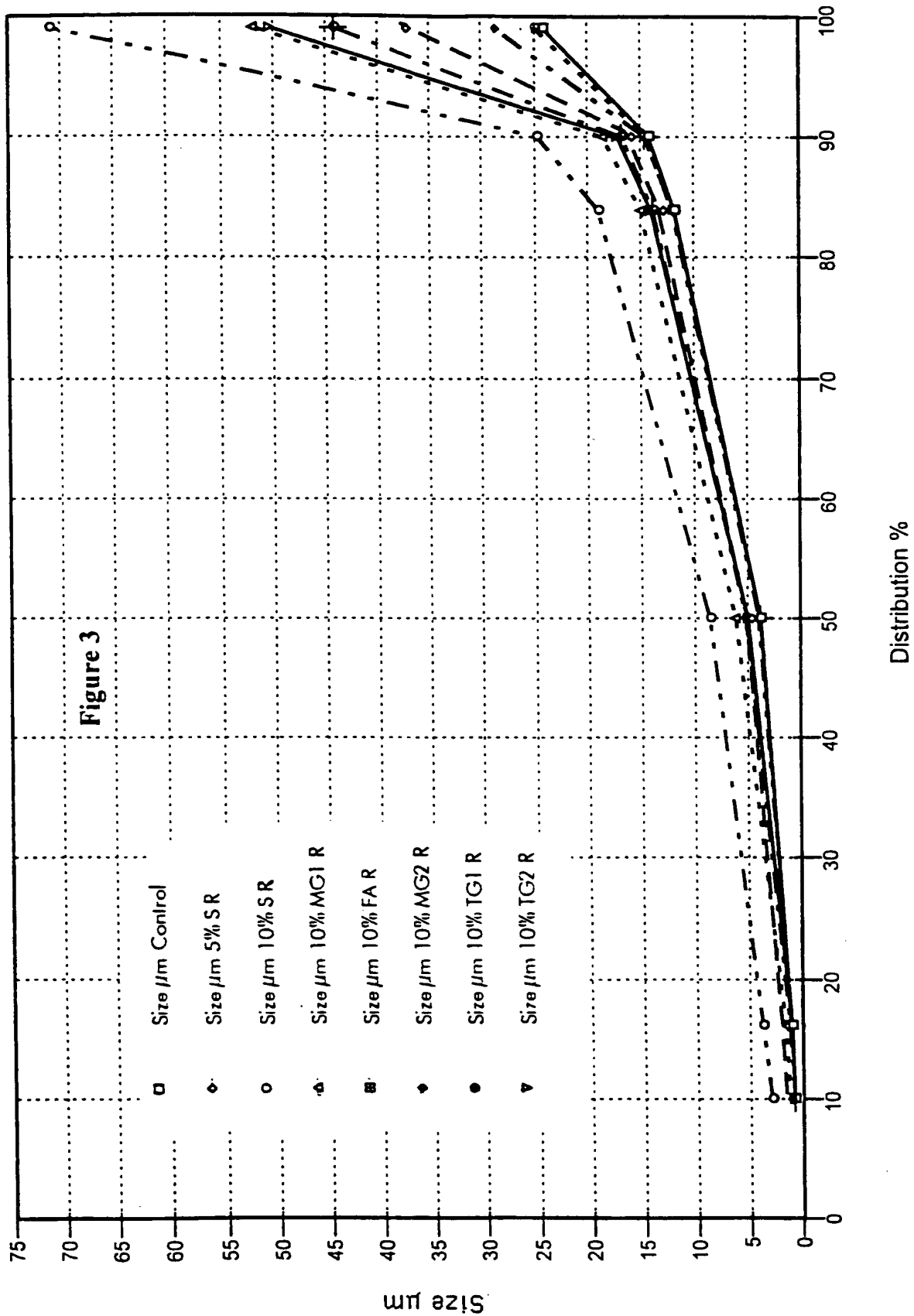
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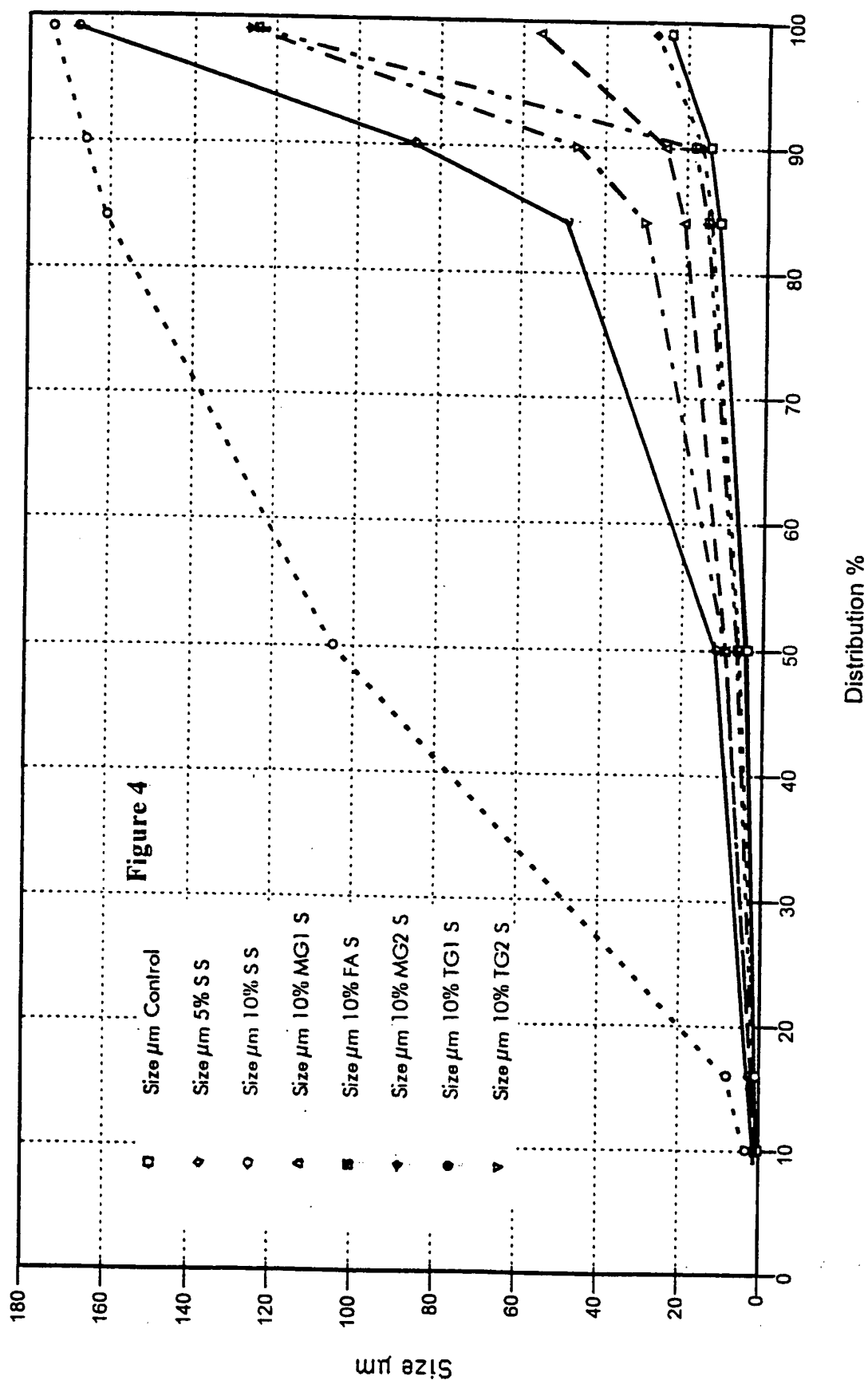
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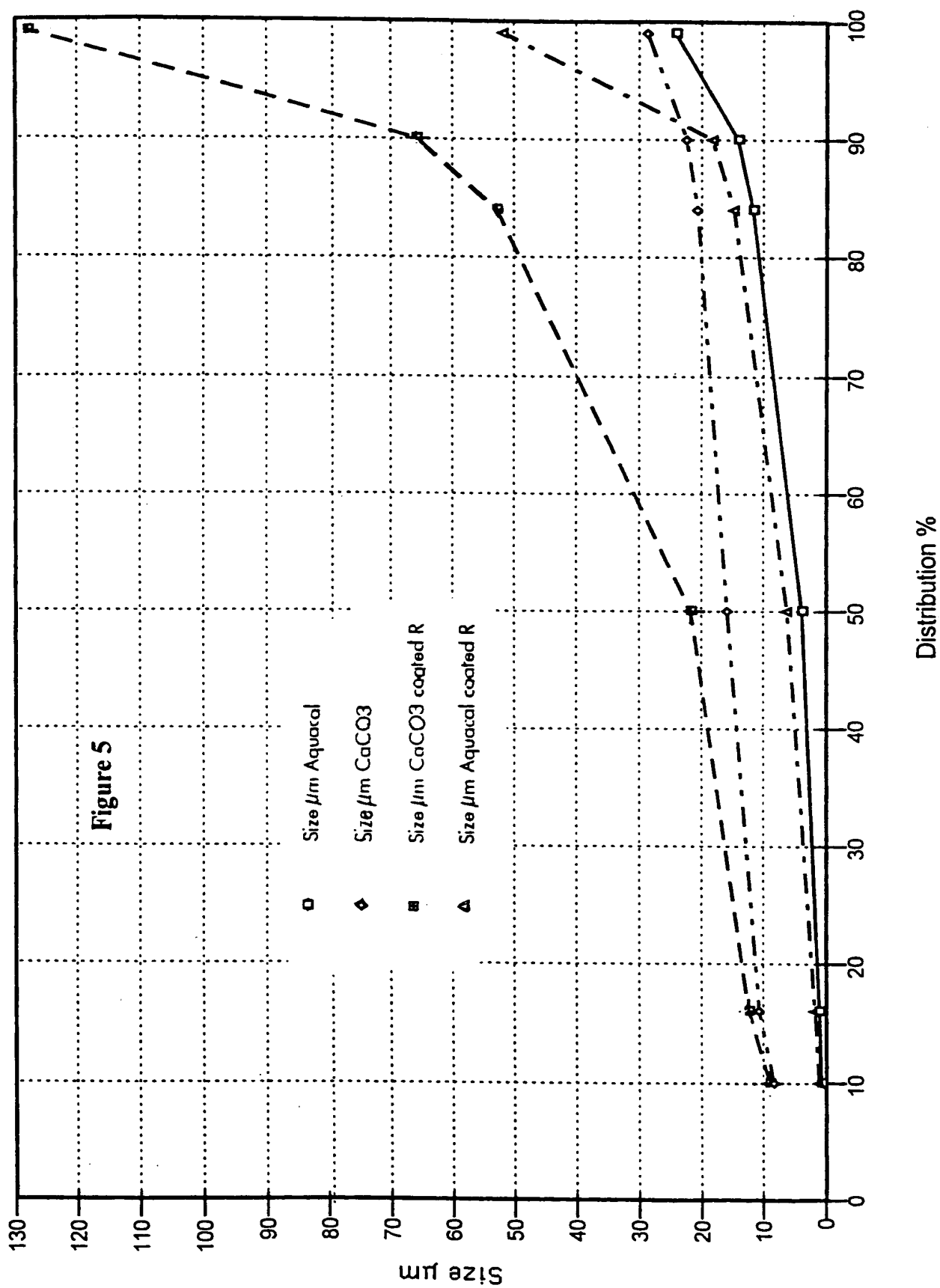
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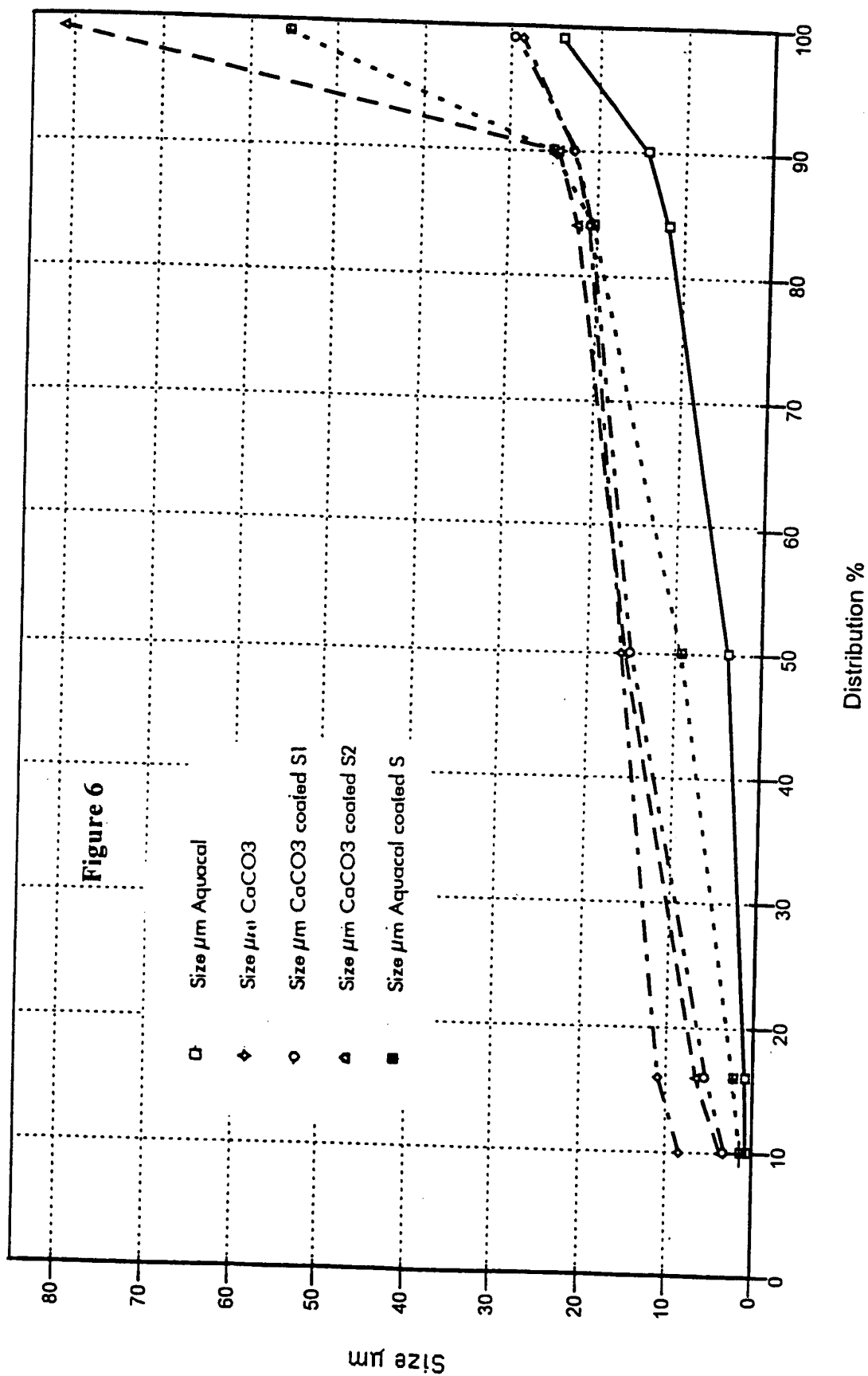












INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 98/00142

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K35/80

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| A | FR 2 201 040 A (SARAP-CEDIA) 26 April 1974 cited in the application ----- | |



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. Application No

PCT/IB 98/00142

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|----------------------------|---------------------|
| FR 2201040 A | 26-04-74 | NONE | |

